REMARKS

Claims 22-33 and 37 are pending in this application. Claims 22, 23, 24, 33 and 37 have been amended. Claims 22-33 and 37 are presented for reconsideration.

Applicants have amended their claims in order to more particularly point out and distinctly claim a preferred aspect of their invention. Thus, the insertion of "C_3-C_5alkyl" into the definition of R_4 in claim 22 is supported by the disclosure on page 5, lines 2-4 and compounds (103) – (106) on pages 25 and 27. The insertion of "C_1-C_6alkylcarbonyl" into said definition of R_4 is supported by the disclosure of compounds (132) – (137) on pages 33-44. The proviso in claim 22 that "when R_4 is hydrogen, R_1 is C_3-C_4 alkyl and R_3 is hydrogen" is supported by the disclosure on page 34 of compounds (139) and (116). Thus no new matter has been added.

The claims presented for consideration embrace a small genus of non- halogenated antimicrobially effective hydroxydiphenyl ether compounds of the formula (1) wherein the phenolic OH is in the meta position with respect to the ether linkage in said formula.

Claims 23-33, 35 and 37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Muntwyler et al. (U.S. Patent 4,268,693) in view of Silverman (The Organic Chemistry of Drug Design and Drug Action, 1992, pages 15-22, in particular Table 2.2 on page 19). However, in the compounds of Muntwyler et al. "each phenyl nucleus contains at least one halogen atom, but the total number of halogen atoms in the molecule does not exceed 4" (col. 1, lines 58-61). The compounds of Muntwyler et al. thus must contain 2, 3 or 4 halogens. Muntwyler et al. therefore clearly *teach away* from halogen-free antimicrobial compounds.

The examiner relies on Silverman's Table 2.2 for the teaching of certain alkyls as isosteres of halogens, in particular F and Cl as isosteres of methyl. Applicants aver that this is a weak "obvious to try" rejection and a completely inadequate basis for making multiple structural changes in the compounds of Muntwyler et al. where polyhalogenation is required, particularly in the absence of any teaching at all in Silverman directed to hydroxydiphenyl ethers. While one might expect that substituting methyl for F and Cl would modify the microbial activity of the compounds disclosed in Muntwyler et al., the most reasonable expectation from the clear teachings of Muntwyler et al. is that they are essential and their removal would destroy said activity! Hence the artisan would not have been motivated to make the multiple structural changes.

Moreover, even if the reference combination were proper, conducting said replacement on any of the disclosed compounds of Muntwyler et al. (compounds (101) – (107) in cols. 11-12), would not give any claimed compound. Every one of these compounds has F or Cl, the isostere of which is methyl, in the position corresponding to R_4. However R_4 as alkyl can only be C_3-C_5alkyl. Hence the narrow genus of compounds presently claimed is distinguished over Muntwyler et al.

Reconsideration and withdrawal of the rejection of claims 23-33 and 37 under 35 U.S.C. § 103(a) as being unpatentable over Muntwyler et al. (U.S. Patent 4,268,693) in view of Silverman is respectfully solicited in light of the remarks *supra*.

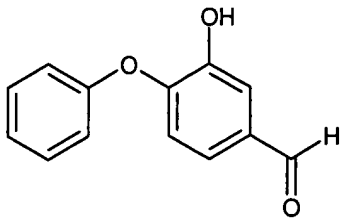
Claims 22-23, 33 and 37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Troesken et al., DE 25 38 016 A1, for the reasons given in the previous office action. The examiner points to a broad generic scope of diphenyl ethers wherein the phenolic OH is always in the para position on page 1 and to compounds 7 and 14 on page 3, and asserts that isomers and adjacent homologues of known compounds in a known method are *prima facie* obvious. However compound 7 on page 3, wherein the phenolic OH is in the para position, is not an isomer or adjacent homologue of any presently claimed compound since claimed R_1 must be C_3-C_4alkyl, not methyl, when R_4 is hydrogen. Hence there are multiple structural differences from any inventive 3-OH compound.

Compound 14 is the only other alkyl-substituted 4-OH diphenyl ether in the 36 reference compounds, most of which are halogenated. There are also multiple structural differences from compound 14 on page 3 with regard to the inventive 3-OH compounds of claim 22 since R_3 as claimed cannot be alkyl when R_4 is hydrogen. In the reference compound it is methyl. Hence, again there are multiple structural differences from the inventive 3-OH compounds. Therefore applicants aver that the narrow genus of compounds presently claimed is distinguished over Troesken et al., DE 25 38 016 A1.

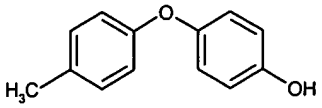
Reconsideration and withdrawal of the rejection of claims 22-23, 33 and 37 under 35 U.S.C. § 103(a) as being unpatentable over Troesken et al., DE 25 38 016 A1, is respectfully solicited in light of the remarks *supra*.

Claims 22, 23 and 33 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fujikawa et al. (abstract of Yakugaku Zasshi, Vol. 91, pp. 930-933, 1971), for the reasons given in the previous office action.

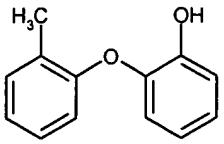
Fujikawa et al. teaches use of certain diphenyl ether compounds as preservatives for sake. The diphenyl ethers of Fujikawa et al. are not taught to be broad-spectrum general purpose antibiotics.

Fujikawa et al. disclose the compound  . There are multiple structural

differences between this compound and the present invention since claimed R_1-R_4 cannot be an aldehyde group and the phenolic hydroxyl must be in the m-position, not the o-position.

Fujikawa et al. also disclose the compound  . However, the phenolic

hydroxyl must be in the m-position, not the p-position in the present invention. Applicants note that Fujikawa's left phenyl moiety has a 4'-methyl radical and no substituent in the o-position, whereas in the instant invention, R_1 (o-position) must be C_3-C_4alkyl, not hydrogen, when R_4 is hydrogen. This compound of Fujikawa et al. has multiple structural differences from the preferred inventive compounds and is therefore not suggestive of them.

Fujikawa et al. also disclose the compound  . However, the phenolic hydroxyl

must be in the m-position, not the o-position in the present invention. Additionally, in the instant invention, R_1 (o-position) must be C_3-C_4alkyl, not methyl, when R_4 is hydrogen. Therefore applicants aver that the narrow genus of compounds presently claimed is distinguished over Fujikawa et al.

Claims 22-25, 27, 30-33 and 37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Leichtlingen et al., U.S. Patent No. 3,753,914, for the reasons given in the previous office action.

Leichtlingen et al. discloses synergistic textile bleaching compositions which may contain an optionally substituted ortho-hydroxydiphenyl ether. While a huge genus of ortho-hydroxydiphenyl ethers is

taught wherein any or all (or none!) of R_1, R_2, R_3, R_4, R_5, R_6, R_7 or R_8 can be a halogen, only R_8, which corresponds to instant R_4, can be an alkyl group, specifically tert. butyl. But, all of the o-hydroxy compounds specifically disclosed in Leichtlingen et al. which have R_8 as tert. butyl, also have a carboxy, carbomethoxy or cyano group in the phenolic hydroxyl ring (all outside the scope of claimed R_4) and from **2 to 5** halogens. Applicants note the examiner has previously acknowledged that there are multiple structural differences from the claimed compounds even prior to the present amendment. This clearly contraindicates the examiner's belief that a prima facie case of obviousness has been shown.

It is well established that hindsight selection from a broad shotgun type disclosure would not guide one skilled in the art to choose appellant's restricted class of compounds from among the host of possible combinations so as to make said class obvious within the meaning of 35 U.S.C. § 103. See *Ex parte Strobel et al.,* 160 USPQ 352 (PTO Bd. of App., 1968), cited with approval numerous times by the CCPA and the CAFC.

Appellants also note *In re Jones*, 21 USPQ 2d 1941, 1943 (CAFC 1992), wherein the Court of Appeals for the Federal Circuit rejected the PTO Commissioner's argument that "regardless how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it". Jones involved an obviousness rejection of a claim to a specific compound, the 2-(2'-aminoethoxy) ethanol salt of 2-methoxy-3,6-dichlorobenzoic acid (dicamba), as obvious in view of, *inter alia*, a prior art reference disclosing a genus which admittedly encompassed the claimed salt. The CAFC reversed the Board's rejection, reasoning that the prior art reference encompassed a "potentially infinite genus" of salts of dicamba and listed several such salts, but that it did not disclose or suggest the claimed salt. Similarly, in *In re Baird*, 29 USPQ 2d 1550, 1552 (CAFC 1994), the court asserted that, while the formula of the Knapp reference unquestionably encompassed bisphenol A when specific variables were chosen, there was nothing in the disclosure of Knapp suggesting that one should select such variables. "A disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds". Quite clearly Leichtlingen et al's disclosure of polyhalogenated o-hydroxydiphenyl ethers indicates a preference leading away from any compounds according to the invention. Hence the subject matter as a whole of all of the rejected claims is unobvious over Leichtlingen et al., U.S. Patent No. 3,753,914.

Reconsideration and withdrawal of the rejection of claims 22-25, 27, 30-33 and 37 under 35 U.S.C. § 103(a) as being unpatentable over Leichtlingen et al., U.S. Patent No. 3,753,914, is respectfully solicited in light of the remarks *supra*.

While independent claim 22 has been argued extensively, all the remaining claims depend on it and further limit it. Hence they are necessarily unobvious.

Since there are no other grounds of objection or rejection, passage of this application to issue with claims 22-33 and 37 is earnestly solicited.

Applicants submit that the present application is in condition for allowance. In the event that minor amendments will further prosecution, Applicants request that the examiner contact the undersigned representative.

Respectfully submitted,

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